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Docket No. 0575/66236/JPW/AJM/DNS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : C. Dominique Toran-Allerand
Serial No. : 10/665,847
Filed : September 19, 2003
For : NOVEL CELL-SURFACE ESTROGEN RECEPTOR AND
RELATED COMPOSITIONS AND METHODS

1185 Avenue of the Americas
New York, New York 10036
September 21, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed on Form PTO-1449 (**Exhibit A**) and are also listed below.

This Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3) before the mailing of a first Office Action on the merits. Thus, this Information Disclosure Statement should be entered and considered. Copies of the documents listed below as items 6-87 are attached hereto as **Exhibits 1-82**.

Pursuant to the Notice appearing in the August 5, 2003 Official Gazette, because this application was filed after June 30, 2003, copies of the U.S. Patents and U.S. Patent Application Publications listed herein are not provided.

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For the convenience of the Examiner, applicants point out that Reference Items 1, 5, 69 and 75 were cited in the June 21, 2004 International Search Report in the corresponding PCT International Application, and a copy of the Report is enclosed as **Exhibit B**.

1. U.S. Patent No. 5,298,429, issued March 29, 1994, Evans et al.;
2. U.S. Patent No. 5,554,601, issued September 10, 1996, Simpkins et al.;
3. U.S. Patent No. 5,843,935, issued December 1, 1998, Simpkins et al.;
4. U.S. Patent No. 6,566,081, issued May 20, 2003, Liao et al.;
5. U.S. Publication No. 2003/0225046, published December 4, 2003, Liao et al.;
6. PCT International Application No. WO 2004/029023, published April 8, 2004 (**Exhibit 1**);
7. Anderson R.G. (1998) The caveolae membrane system. Annu. Rev. Biochem. 67:199-225 (**Exhibit 2**);
8. Anuradha P., Khan S.M., Karthikeyan N., and Thampan R.V. (1994) The nonactivated estrogen receptor (naER) of the goat uterus is a tyrosine kinase. Arch. Biochem. Biophys. 309:195-204 (**Exhibit 3**);

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9. Arnold L.E., (1996) Sex differences in ADHD: conference summary. J. Abnorm. Child. Psychol. 24:555-569 (**Exhibit 4**);
10. Aronica S.M., Kraus W.L., and Katzenellenbogen B.S. (1994) Estrogen action via the cAMP signaling pathway: stimulation of adenylate cyclase and cAMP-regulated gene transcription. Proc. Natl. Acad. Sci. USA 91:8517-8521 (**Exhibit 5**);
11. Beato M., and Klug J. (2000) Steroid hormone receptors: an update. Hum. Reprod. Update 6:225-236 (**Exhibit 6**);
12. Behl C., Skutella T., Lezoualc'h F., Post A., Widmann M., Newton J., and Holsboer F. (1997) Neuroprotection against oxidative stress by estrogens: structure-activity relationship. Mol. Pharmacol. 51:535-541 (**Exhibit 7**);
13. Benten W.P., Stephan C., Lieberherr M., and Wunderlich F. (2001) Estradiol signaling via sequestrable surface receptors. Endocrinology 142(4):1669-1677 (**Exhibit 8**);
14. Bickel P.E., Scherer P.E., Schnitzer J.E., Oh P., Lisanti M.P. and Lodish H.F. (1997) Flotillin and epidermal surface antigen define a new family of caveolae-associated integral membrane proteins. J. Biol. Chem. 272:13793-13802 (**Exhibit 9**);
15. Blaustein J.D. (1992) Cytoplasmic estrogen receptors in rat brain: immunocytochemical evidence using three antibodies with distinct epitopes. Endocrinology 131:1336-1342 (**Exhibit 10**);

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Page 4

16. Clark A.S., and Goldman-Rakic P. (1989) Gonadal hormones influence the emergence of cortical function in nonhuman primates. Behav. Neurosci. 103:1287-1295 (**Exhibit 11**);
17. Das S.K., Taylor J.A., Korach K.S., Paria B.C., Dey S.K., and Lubahn D.B. (1997) Estrogenic responses in estrogen receptor-alpha deficient mice reveal a distinct estrogen signaling pathway. Proc. Natl. Acad. Sci. U.S.A 94:12786-12791 (**Exhibit 12**);
18. Dubal D.B., Zhu H., Yu J., Rau S.W., Shughrue P.J., Merchenthaler I., Kindy M.S., and Wise P.M. (2001) Estrogen receptor alpha, not beta, is a critical link in estradiol-mediated protection against brain injury. Proc. Natl. Acad. Sci. U.S.A 98:19552-19577 (**Exhibit 13**);
19. Filardo E.J., Quinn J.A., Bland K.I. and Frackelton A.R. Jr. (2000) Estrogen-induced activation of Erk-1 and Erk-2 requires the G protein-coupled receptor homologue, GPR30, and occurs via trans-activation of the epidermal growth factor receptor through release of HB-EGF. Mol. Endocrinol. 14:1649-1660 (**Exhibit 14**);
20. Fitzpatrick S.L., Funkhouser J.M., Sindoni D.M., Stevis P.E., Deecher D.C., Bapat A.R., Merchenthaler I., and Frail D.E. (1999) Expression of estrogen receptor-beta protein in rodent ovary. Endocrinology 140:2581-2591 (**Exhibit 15**);
21. Friend K.E., Resnick E.M., Ang L.W., and Shupnik M.A. (1997) Specific modulation of estrogen receptor mRNA isoforms in rat

- pituitary throughout the estrous cycle and in response to steroid hormones. Mol. Cell Endocrinol. 131:147-155 (**Exhibit 16**);
22. Garcia-Segura L.M., Olmos G. Tranque P. and Naftolin F. (1987) Rapid effects of gonadal steroids upon hypothalamic neuronal membrane ultrastructure. J. Steroid Biochem. 27:615-623 (**Exhibit 17**);
 23. Garcia-Segura L.M., Azcoitia I., and DonCarlos L.L. (2001) Neuroprotection by estradiol. Prog. Neurobiol. 63:29-60 (**Exhibit 18**);
 24. Gerlach J., McEwen B.S., Toran-Allerand C.D. and Friedman W.J. (1983) Perinatal development of estrogen receptors in mouse brain assessed by radioautography, nuclear isolation and receptor assay. Develop. Brain Res. 11:7-18 (**Exhibit 19**);
 25. Geschwind N., and Behan P.O. (1982) Left-handedness: association with immune disease, migraine and developmental learning disorders. Proc. Natl. Acad. Sci. USA 7:5097-5100 (**Exhibit 20**);
 26. Green P.S., Bishop J., and Simpkins J.W. (1997) 17alpha-estradiol exerts neuroprotective effects on SK-N-SH cells. J. Neurosci. 17:511-515 (**Exhibit 21**);
 27. Green P.S., and Simpkins J.W. (2000) Neuroprotective effects of estrogens: potential mechanisms of action. Int. J. Dev. Neurosci. 18:347-358 (**Exhibit 22**);
 28. Gu Q., Korach K.S., and Moss R.L. (1999) Rapid action of 17beta-estradiol on kainate-induced currents in hippocampal neurons lacking intracellular estrogen receptors. Endocrinology 140:660-666 (**Exhibit 23**);

29. Guo Z., Krucken J., Benten W.P., Wunderlich F. (2002) Estradiol-induced nongenomic calcium signaling regulates genotropic signaling in macrophages. *J. Biol. Chem.* 277:7044-7050 (**Exhibit 24**);
30. Hawkins M.B., Thornton J.W., Crews D., Skipper J.K., Dotte A., and Thomas P. (2000) Identification of a third distinct estrogen receptor and reclassification of estrogen receptors in teleosts. *Proc. Natl. Acad. Sci. USA* 97:10751-10756 (**Exhibit 25**);
31. Huang C.S., Zhou J., Feng A.K., Lynch C., Klumperman J., DeArmond S.J., and Mobley W.C. (1999) Nerve growth factor signaling in caveolae-like domains at the plasma membrane. *J. Biol. Chem.* 274:36707-36714 (**Exhibit 26**);
32. Huang J., Choudhri T.F., Winfree C.J., McTaggart R.A., Kiss S., Mocco J., Kim L.J., Protopsaltis T.S., Zhang Y., Pinsky D.J., and Connolly E.S. Jr. (2000) Postischemic cerebrovascular E-selectin expression mediates tissue injury in murine stroke. *Stroke* 31:3047-3053 (**Exhibit 27**);
33. Iwabuchi K., Handa K., and Hakomori S. (2000) Separation of glycosphingolipid-enriched microdomains from caveolar membrane characterized by presence of caveolin. *Methods Enzymol.* 312:488-494 (**Exhibit 28**);
34. Jones E.G. (1995) Cortical development and neuropathology in schizophrenia. *Ciba. Found. Symp.* 193:277-295 (**Exhibit 29**);

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35. Karthikeyan N., and Thampan R.V. (1996) Plasma membrane is the primary site of localization of the nonactivated estrogen receptor in the goat uterus: hormone binding causes receptor internalization. Arch. Biochem. Biophys. 325:47-57 (**Exhibit 30**);
36. Kelly M.J., Moss R.L., and Dudley C.A. (1978) The effect of ovariectomy on the responsiveness of preoptic-septal neurons to microelectrophoresed estrogen. Neuroendocrin. 25:204-211 (**Exhibit 31**);
37. Kelly M.J., and Wagner E.J. (1999) Estrogen Modulation of G-protein-coupled Receptors. Trends Endocrinol. Metab. 10:369-374 (**Exhibit 32**);
38. Kuiper G.G., Enmark E., Peltö-Huikko M., Nilsson S., and Gustafsson J.A. (1996) Cloning of a novel receptor expressed in rat prostate and ovary. Proc. Natl. Acad. Sci. U.S.A 93:5925-5930 (**Exhibit 33**);
39. Kuiper G.G., Carlsson B., Grandien K., Enmark E., Haggblad J., Nilsson S., and Gustafsson J.A. (1997) Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors alpha and beta. Endocrinology 138:863-870 (**Exhibit 34**);
40. Landers J.P., and Spelsberg T.C. (1992) New concepts in steroid hormone action: Transcription factors, proto-oncogenes and the cascade model for steroid regulation of gene expression. Crit. Rev. Eukaryotic Gene Expression 2:19-63 (**Exhibit 35**);
41. Levin E.R. (2002) Cellular functions of plasma membrane estrogen receptors. Steroids. 67:471-475 (**Exhibit 36**);

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42. Liu P., Ying Y.S. and Anderson R.G.W. (1997) Platelet-derived growth factor activates mitogen-activated protein kinase in isolated caveolae. Proc. Natl. Acad. Sci. USA 94: 13666-13670 (**Exhibit 37**);
43. Lubahn D.B., Moyer J.S., Golding T.S., Couse J.F., Korach K.S., and Smithies O. (1993) Alteration of reproductive function but not prenatal sexual development after insertional disruption of the mouse estrogen receptor gene. Proc. Natl. Acad. Sci. U.S.A 90:1162-1166 (**Exhibit 38**);
44. MacLusky N.J., Naftolin F., Goldman-Rakic P.S. (1986) Estrogen formation and binding in the cerebral cortex of the developing rhesus monkey. Proc. Natl. Acad. Sci. USA 83:513-516 (**Exhibit 39**);
45. Marino M., Distefano E., Trentalance A., and Smith C.L. (2001) Estradiol-induced IP(3) mediates the estrogen receptor activity expressed in human cells. Mol. Cell. Endocrinol. 182:19-26 (**Exhibit 40**);
46. Marshall C.J. (1995) Specificity of receptor tyrosine kinase signaling: transient versus sustained extracellular signal-regulated kinase activation. Cell. 80:179-185 (**Exhibit 41**);
47. Matsumoto A., and Arai Y. (1981) Neuronal plasticity in the deafferented hypothalamic arcuate nucleus of adult female rats and its enhancement by treatment with estrogen. J. Comp. Neurol. 197:197-205 (**Exhibit 42**);

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48. Milner T.A., McEwen B.S., Hayashi S., Li C.J., Reagan L.P. and Alves S.E. (2001) Ultrastructural evidence that hippocampal alpha estrogen receptors are located at extranuclear sites. J. Comp. Neurol. 429:355-371 (**Exhibit 43**);
49. Nadal A., Ropero A.B., Laribi O., Maillet M., Fuentes E., and Soria B. (2000) Nongenomic actions of estrogens and xenoestrogens by binding at a plasma membrane receptor unrelated to estrogen receptor alpha and estrogen receptor beta. Proc. Natl. Acad. Sci. U.S.A 97:11603-11608 (**Exhibit 44**);
50. Nethrapalli I.S., Singh M., Guan X., Guo Q.F., Lubahn D.B., Korach K.S. and Toran-Allerand C.D. (2001) Estradiol (E2) Elicits Src Phosphorylation in Mouse Neocortex: The Initial Event in E2 Activation of the MAPK Cascade? Endocrinology 142:5145-5148 (**Exhibit 45**);
51. Okamoto T., Schlegel A., Scherer P.E., and Lisanti M.P. (1998) Caveolins, a family of scaffolding proteins for organizing "pre-assembled signaling complexes" at the plasma membrane. J. Biol. Chem. 273:5419-5422 (**Exhibit 46**);
52. Pennington B.F., Heaton R.K., Karzmark P., Pendleton M.G., Lehman R., and Shucard D.W. (1985) The neuropsychological phenotype in Turner syndrome. Cortex 21:391-404 (**Exhibit 47**);
53. Petersen D.N., Tkalcevic G.T., Koza-Taylor P.H., Turi T.G., and Brown T.A. (1998) Identification of estrogen receptor beta2, a functional variant of estrogen receptor beta expressed in normal rat tissues. Endocrinology 139:1082-1092 (**Exhibit 48**);

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54. Razandi M., Pedram A., Greene G.L., and Levin E.R. (1999) Cell membrane and nuclear estrogen receptors (ERs) originate from a single transcript: studies of ER- α and ER- β expressed in Chinese hamster ovary cells. Mol. Endocrinol. 13:307-319 (**Exhibit 49**);
55. Razandi M., Oh P., Pedram A., Schnitzer J., and Levin E.R. (2002) ERs associate with and regulate the production of caveolin: implications for signaling and cellular actions. Mol. Endocrinol. 16:100-115 (**Exhibit 50**);
56. Ros-Baro A., Lopez-Iglesias C., Peiro S., Bellido D., Palacin M., Zorzano A., and Camps M. (2001) Lipid rafts are required for GLUT4 internalization in adipose cells. Proc. Natl. Acad. Sci. USA 98:12050-12055 (**Exhibit 51**);
57. Rothberg K.G., Ying Y.S., Kamen B.A., and Anderson R.G. (1990) Cholesterol controls the clustering of the glycopospholipid-anchored membrane receptor for 5-methyltetrahydrofolate. J. Cell Biol. 111:2931-2938 (**Exhibit 52**);
58. Schlegel A., Volonte D., Engelman J.A., Galbiati F., Mehta P., Zhang X.L., Scherer P.E., and Lisanti M.P. (1998) "Crowded little caves": structure and function of caveolae. Cell Signal. 10:457-63 (**Exhibit 53**);
59. Schreihof D.A., Resnick E.M., Soh A.Y., and Shupnik M.A. (1999) Transcriptional regulation by a naturally occurring truncated rat estrogen receptor (ER), truncated ER product-1 (TERP-1). Mol. Endocrinol. 13:320-329 (**Exhibit 54**);

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60. Schupf N., and Sergievsky G.H. (2002) Genetic and host factors for dementia in Down's syndrome. Br. J. Psychiatry. 180:405-410 **(Exhibit 55);**
61. Sétáló G. Jr., Singh M., Guan X., and Toran-Allerand C.D. (2001) Estradiol-induced phosphorylation of ERK $\frac{1}{2}$ in explants of the mouse cerebral cortex: the roles of heat shock protein 90 (Hsp90) and MEK2. J. Neurobiol. 50:1-12 **(Exhibit 56);**
62. Shughrue P.J., Lane M.V., and Merchenthaler I. (1997) Comparative distribution of estrogen receptor-alpha and -beta mRNA in the rat central nervous system. J. Comp. Neurol. 388:507-525 **(Exhibit 57);**
63. Shughrue P.J., Askew G.R., Dellovade T.L., and Merchenthaler I. (2002) Estrogen-binding sites and their functional capacity in estrogen receptor double knockout mouse brain. Endocrinology 143:1643-1650 **(Exhibit 58);**
64. Singer C.A., Figueroa-Masot X.A., Batchelor R.H., and Dorsa D.M. (1999) The mitogen-activated protein kinase pathway mediates estrogen neuroprotection after glutamate toxicity in primary cortical neurons. J. Neurosci. 19:2455-2463 **(Exhibit 59);**
65. Singh M., Sétáló Jr. G., Guan X., Warren M., and Toran-Allerand C.D. (1999) Estrogen-induced activation of MAP Kinase (ERK) in cerebral cortical explants: Convergence of estrogen and neurotrophin signaling pathways. J. Neurosci. 19:1179-1188 **(Exhibit 60);**
66. Singh M., Sétáló Jr. G., Guan X., Frail D.F., and Toran-Allerand C.D. (2000) Estrogen-induced activation of the MAP kinase cascade in the cerebral cortex of estrogen receptor- α knock-out mice. J. Neurosci. 20:1694-1700 **(Exhibit 61);**

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67. Smart E.J., Ying Y.S., Mineo C., and Anderson R.G. (1995) A detergent-free method for purifying caveolae membrane from tissue culture cells. Proc. Natl. Acad. Sci. U.S.A 92:10104-10108 (**Exhibit 62**);
68. Stauffer S.R., Coletta C.J., Tedesco R., Nishiguchi G., Carlson K., Sun J., Katzenellenbogen B.S., and Katzenellenbogen J.A. (2000) Pyrazole ligands: Structure-affinity/activity relationships and estrogen receptor- α selective agonists. J. Med. Chem. 43:4934-4947 (**Exhibit 63**);
69. Stefano G.B. et al. (2000) Cell-Surface Estrogen Receptors Mediate Calcium-Dependent Nitric Oxide Release in Human Endothelia. Career and Technical Education. Circulation 1594-1597 (**Exhibit 64**);
70. Strauss E., Wada J., and Hunter M. (1992) Sex-related differences in the cognitive consequences of early left hemisphere lesions. J. Clin. Exp. Neuropsychol. 14:738-748 (**Exhibit 65**);
71. Subtil A., Gaidarov I., Kobylarz K., Lampson M.A., Keen J.H., and McGraw T.E. (1999) Acute cholesterol depletion inhibits clathrin-coated pit budding. Proc. Natl. Acad. Sci. USA 96:6775-6780 (**Exhibit 66**);
72. Sukovich D.A., Mukherjee R., and Benfield P.A. (1994) A novel, cell-type-specific mechanism for estrogen receptor-mediated gene activation in the absence of an estrogen-responsive element. Mol. Cell. Biol. 14:7134-7143 (**Exhibit 67**);

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73. Tallal P., and McEwen B. (1991b) Neuroendocrine effects on brain development and cognition. *Psychoneuroendocrinology* 16:3-6 (**Exhibit 68**);
74. Tang M.X., Jacobs D., Stern Y., Marder K., Schofield P., Gurland, Andrews H., and Mayeux R. (1996) Effect of oestrogen during menopause on risk and age at onset of Alzheimer's disease. *Lancet* 348:429-432 (**Exhibit 69**);
75. Thornton M.J., (2002) The Biological Actions of Estrogens on Skin. *Experimental Dermatology* 11:487-502 (**Exhibit 70**);
76. Toran-Allerand C.D. (1976) Sex steroids and the development of the newborn mouse hypothalamus and preoptic area *in vitro*: Implications for sexual differentiation. *Brain Res.* 106:407-412 (**Exhibit 71**);
77. Toran-Allerand CD (1980) Sex steroids and the development of the newborn mouse hypothalamus and preoptic area *in vitro*: II. Morphological correlates and hormonal specificity. *Brain Res.* 189:413-427 (**Exhibit 72**);
78. Toran-Allerand C.D., Miranda R.C., Hochberg R.B., and MacLusky N.J. (1992) Cellular variations in estrogen receptor mRNA translation in the developing brain: Evidence from combined ¹²⁵I-estrogen autoradiography and non-isotopic *in situ* hybridization histochemistry. *Brain Res.* 576:25-41 (**Exhibit 73**);
79. Toran-Allerand C.D., Singh M., and Sétáló Jr. G. (1999) Novel Mechanisms of Estrogen Action in the Brain: New players in an old story. *Frontiers in Neuroendocrinology* 20:97-121 (**Exhibit 74**);

80. Toran-Allerand C.D. (2000) Novel sites and mechanisms of oestrogen action in the brain. In: Neuronal and Cognitive Effects of Oestrogens, Wiley, Chichester (Novartis Foundation Symposium 230), pages 56-73 (**Exhibit 75**);
81. Tremblay G.B., Tremblay A., Copeland N.G., Gilbert D.J., Jenkins N.A., Labrie F., and Giguere V. (1997) Cloning, chromosomal localization, and functional analysis of the murine estrogen receptor beta. Mol. Endocrinol. 11:353-365 (**Exhibit 76**);
82. Tsuchiya K., Ikeda K., Niizato K., Watabiki S., Anno M., Taki K., Haga C., Iritani S., and Matsushita M. (2002) Parkinson's disease mimicking senile dementia of the Alzheimer type: a clinicopathological study of four autopsy cases. Neuropathology 22:77-84 (**Exhibit 77**);
83. Wade C.B., Robinson S., Shapiro R.A., and Dorsa D.M. (2001) Estrogen receptor (ER)alpha and ERbeta exhibit unique pharmacologic properties when coupled to activation of the mitogen-activated protein kinase pathway. Endocrinology 142:2336-2342 (**Exhibit 78**);
84. Watson C.S., Norfleet A.M., Pappas T.C., and Gametchu B. (1999) Rapid actions of estrogens in GH3/B6 pituitary tumor cells via a plasma membrane version of estrogen receptor-alpha. Steroids 64:5-13 (**Exhibit 79**);
85. Watson F.L., Heerssen H.M., Bhattacharyya A., Klesse L., Lin M.Z., and Segal R.A. (2001) Neurotrophins use the Erk5 pathway to mediate

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a retrograde survival response. Nat Neurosci. 4:981-988 (**Exhibit 80**);

86. Watters J.J., Campbell J.S., Cunningham M.J., Krebs E.G., and Dorsa D.M. (1997) Rapid membrane effects of steroids in neuroblastoma cells: effects of estrogen on mitogen activated protein kinase signalling cascade and c-fos immediate early gene transcription. Endocrinology 138:4030-4033 (**Exhibit 81**); and
87. Wyckoff M.H., Chambliss K.L., Mineo C., Yuhanna I.S., Mendelsohn M.E., Mumby S.M., and Shaul P.W. (2001) Plasma membrane estrogen receptors are coupled to endothelial nitric-oxide synthase through Galpha(i). J. Biol. Chem. 276:27071-27076 (**Exhibit 82**).

Applicants request that the Examiner review the references and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

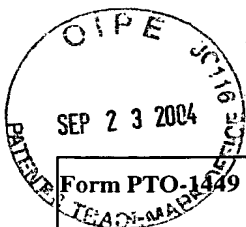
Respectfully submitted,

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Alan J. Morrison
Reg. No. 37,399

Date

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Serial No.

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INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Applicants:

C. Dominique Toran-Allerand

Filing Date

September 19, 2003

Group

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	5 2 9 8 4 2 9	3/29/94	Evans et al.;			
	5 5 5 4 6 0 1	9/10/96	Simpkins et al.;			
	5 8 4 3 9 3 5	12/1/98	Simpkins et al.;			
	6 5 6 6 0 8 1	5/20/03	Liao et al.;			
	20 03 02 5 0 4 6	12/4/03	Liao et al.;			

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
					Yes No
WO 20 04 02 9 0 2 3	4/8/04	PCT;			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Anderson R.G. (1998) The caveolae membrane system. Annu. Rev. Biochem. 67:199-225 ;
	Anuradha P., Khan S.M., Karthikeyan N., and Thampan R.V. (1994) The nonactivated estrogen receptor (naER) of the goat uterus is a tyrosine kinase. Arch. Biochem. Biophys. 309:195-204;
	Arnold L.E., (1996) Sex differences in ADHD: conference summary. J. Abnorm. Child. Psychol. 24:555-569;
	Aronica S.M., Kraus W.L., and Katzenellenbogen B.S. (1994) Estrogen action via the cAMP signaling pathway: stimulation of adenylate cyclase and cAMP-regulated gene transcription. Proc. Natl. Acad. Sci. USA 91:8517-8521
	Beato M., and Klug J. (2000) Steroid hormone receptors: an update. Hum. Reprod. Update 6:225-236;
	Behl C., Skutella T., Lezoualc'h F., Post A., Widmann M., Newton J., and Holsboer F. (1997) Neuroprotection against oxidative stress by estrogens: structure-activity relationship. Mol. Pharmacol. 51:535-541;
	Benten W.P., Stephan C., Lieberherr M., and Wunderlich F. (2001) Estradiol signaling via sequestrable surface receptors. Endocrinology 142(4):1669-1677;
	Bickel P.E., Scherer P.E., Schnitzer J.E., Oh P., Lisanti M.P. and Lodish H.F. (1997) Flotillin and epidermal surface antigen define a new family of caveolae-associated integral membrane proteins. J. Biol. Chem. 272:13793-13802;
	Blaustein J.D. (1992) Cytoplasmic estrogen receptors in rat brain: immunocytochemical evidence using three antibodies with distinct epitopes. Endocrinology 131:1336-1342;
	Clark A.S., and Goldman-Rakic P. (1989) Gonadal hormones influence the emergence of cortical function in nonhuman primates. Behav. Neurosci. 103:1287-1295;

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Exhibit A

Form PTO-1449		U.S. Department of Commerce Patent and Trademark Office			Atty. Docket No. 66236/JPW/AJM/DNS		Serial No. 10/608,841	
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)					Applicants: C. Dominique Toran-Allerand			
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